DEPARTMENT OF HEALTH & HUMAN SERVICES

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NOV 26 1999

Food and Drug Administration
Rockville MD 20857

WARNING LETTER

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Reference No:99-HFD-45-11-01

Joseph F. Holson, Ph.D.
President
WIL Research Laboratories, Inc.
1407 George Road
Ashland, OH 44805-9281

Dear Dr. Holson:

During November of 1998 and January of 1999, Mr. Frederick M. Lochner, investigator from the Food and Drug Administration (FDA), visited WIL Research nonclinical laboratory facilities to assess adherence to the Good Laboratory Practice (GLP) regulations, Title 21, Code of Federal Regulations, Part 58. Studies [ ] were also audited during this time.

During the inspection, our investigator observed a number of deviations from the GLP regulations. The deficiencies were listed on a Form FDA 483 which was discussed with and presented to you and other representatives of WIL Research Laboratories at the conclusion of the inspection. We have reviewed Ms. [ ] letter, dated January 20, 1999, responding to the FDA 483. In addressing our concerns, WIL Research promised corrections to only a few of the violative findings. The explanations for not committing to correct other findings did not satisfy our concerns.

Your response indicates that none of the FDA 483 observations suggest non-compliance with the GLP regulations. The response also indicates that, as a contract laboratory, WIL Research cannot be held responsible for sponsor conducted activities (analyses of dosing formulations) which are not under WIL Research's direct control. This response does not satisfy the requirements as set forth in Section 58.31(d) of the Good Laboratory Practice regulations which requires that testing facility management shall assure that test and control articles or mixtures have been appropriately tested. Specifically, when analytical tests for homogeneity, concentration, and stability of dosing formulations are performed by another laboratory, it is the testing facility's responsibility to assure that such tests are performed, and that dosing formulations, including solutions and resuspensions, are homogeneous and appropriately tested. WIL Research did not fulfill these requirements. Moreover, the response did not assure that SOPs would be followed in the employment of HPLC columns; that aseptic procedures for the production of dosing formulations would be validated; and that certain dosing formulations would be tested for pyrogens and sterility.

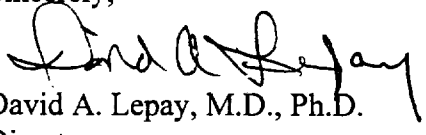
This letter is notification that the FDA may refuse to consider any particular nonclinical laboratory study in support of an application for a research or marketing permit, if it finds that the study was not conducted in accordance with the Good Laboratory Practice regulations. Prior to initiation of any further new nonclinical laboratory studies, the observed GLP deficiencies must be corrected and you should request from the FDA Cincinnati District Office that your laboratory be reinspected.

Please notify this office in writing within fifteen (15) working days of receipt of this letter and indicate your intentions to immediately correct the GLP violations, and/or assure the Agency that you will conduct no further studies which are subject to the GLP regulations until corrections are made and verified.

If you have any questions concerning these matters, or the Good Laboratory Practice regulations, please contact:

C.T. Viswanathan, Ph.D.
Associate Director (Bioequivalence)
Chief, GLP and Bioequivalence Investigations Branch
Division of Scientific Investigations
Office of Medical Policy
Center for Drug Evaluation and Research
7520 Standish Place, Room 151
Rockville, MD 20855
Telephone: (301) 827-5460

Sincerely,



David A. Lepay, M.D., Ph.D.
Director
Division of Scientific Investigations
Center for Drug Evaluation and Research

cc:[ ]
WIL Research Laboratories, Inc.